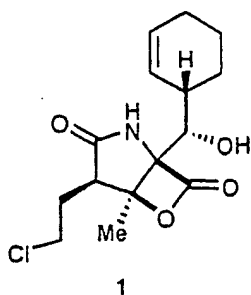


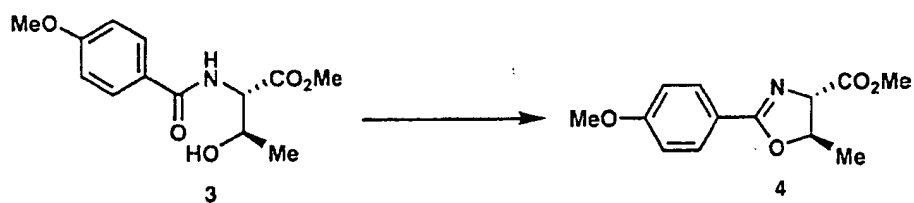
WHAT IS CLAIMED IS:

1. A process for the enantiospecific total synthesis of the compound of structure 1:

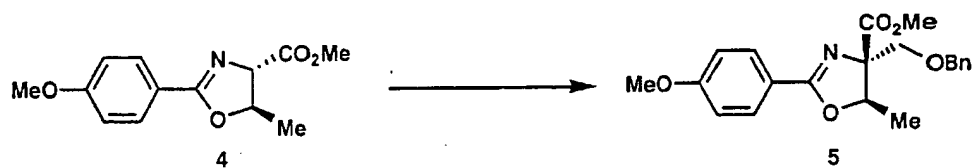


comprising the steps of:

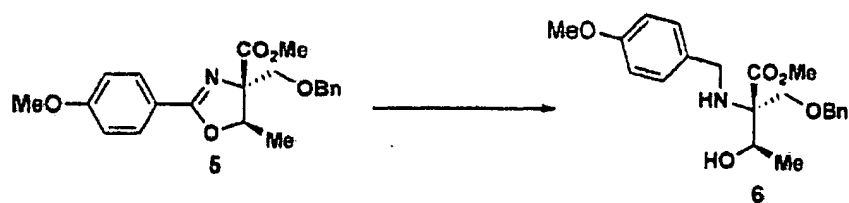
- (a) converting amide 3 to oxazoline 4:



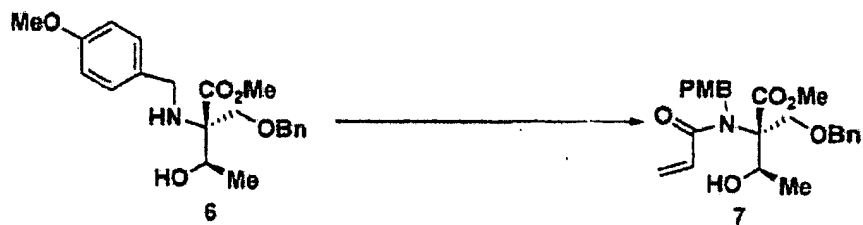
- (b) deprotonating 4 followed by alkylation of the resulting enolate to provide 5:



- (c) reducing 5 to yield the N-4-methoxybenzylamine 6:



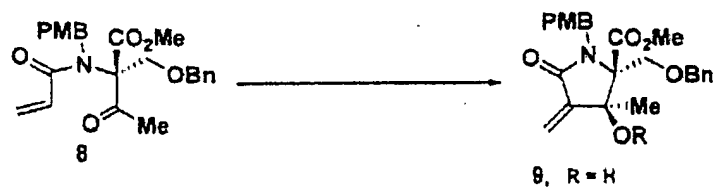
(d) acylating 6a (structure not shown, OH in 6 is OTMS) to afford the N-acrylyl-N-PMB derivative 7:



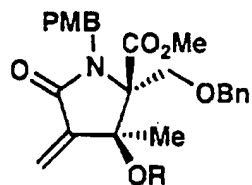
(e) oxidizing 7 to produce the keto amide ester 8:



(f) cyclizing 8 to afford the  $\gamma$ -lactam 9:

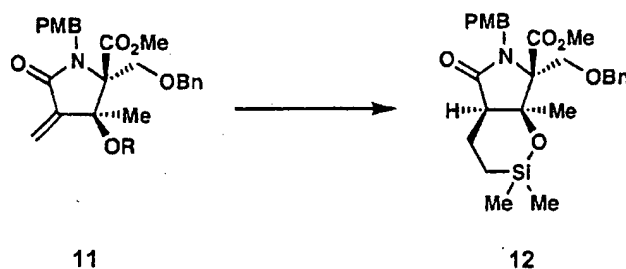


- (g) silylating **9** to produce the silyl ether **11**:

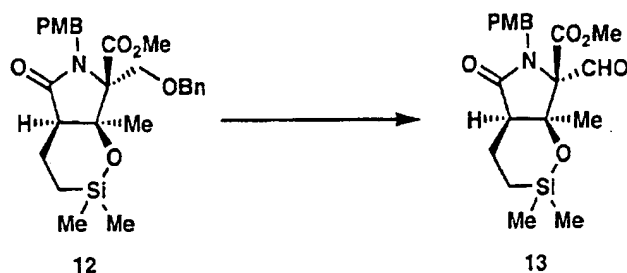


**9**, R = H  
**11**, R = Si(Me)<sub>2</sub>CH<sub>2</sub>Br

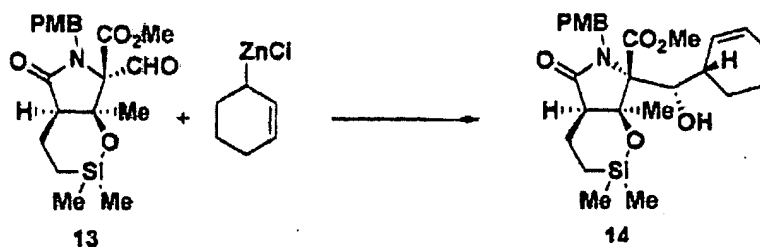
- (h) cyclizing **11** to provide the *cis*-fused  $\gamma$ -lactam **12**:



- (i) cleaving the protecting group (OBn) in compound **12** to yield the primary alcohol **12a** (wherein OBn in **12** is OH), and oxidizing **12a** to provide the aldehyde **13**:



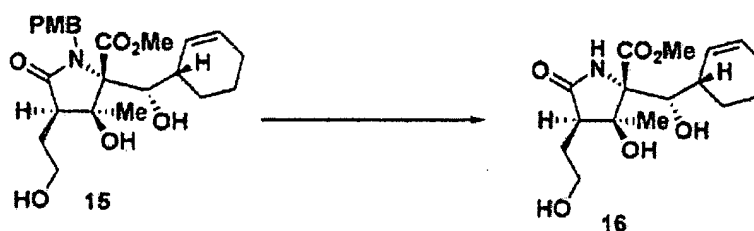
- (j) reacting 2-cyclo-hexenylzinc chloride with the aldehyde **13** to yield the formyl adduct **14**:



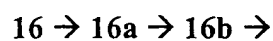
(k) oxidizing 14 to provide the triol 15:

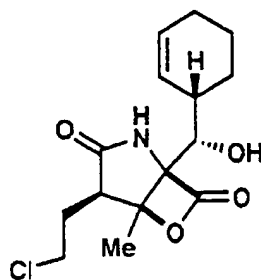


(l) cleaving the PMB group of 15 to yield the triol ester 16:



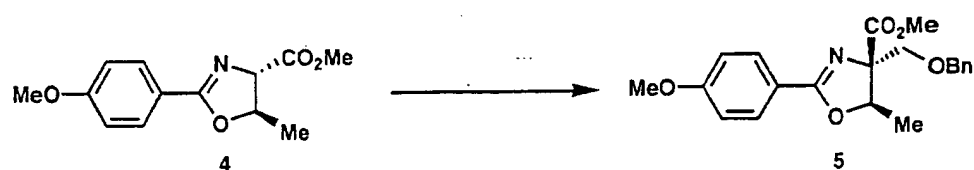
(m) hydrolyzing 16 to the corresponding  $\gamma$ -lactam-carboxylic acid 16a ( $\text{CO}_2\text{Me}$  in 16 is  $\text{CO}_2\text{H}$ ), followed by conversion of the acid 16a to the beta-lactone 16b, followed by conversion to salinosporamide A (1):



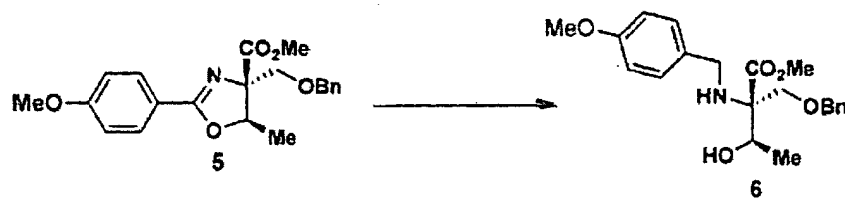


1

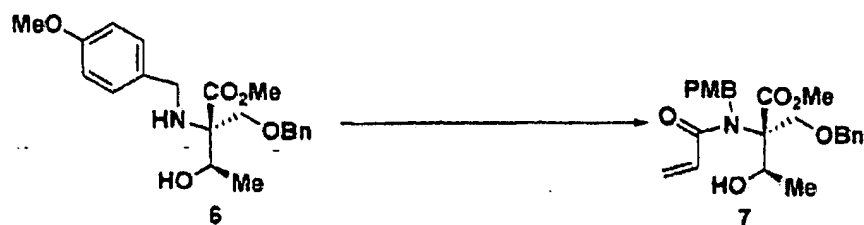
2. The intermediate step (b) of Claim 1, namely the deprotonation of 4 followed by alkylation of the resulting enolate to provide 5:



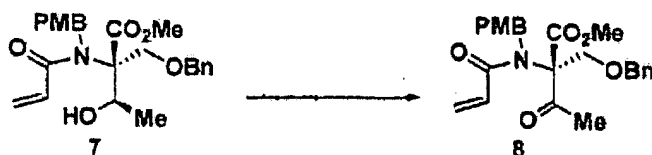
3. The intermediate step (c) of Claim 1, namely the reduction of 5 to yield the N-4-methoxybenzylamine 6:



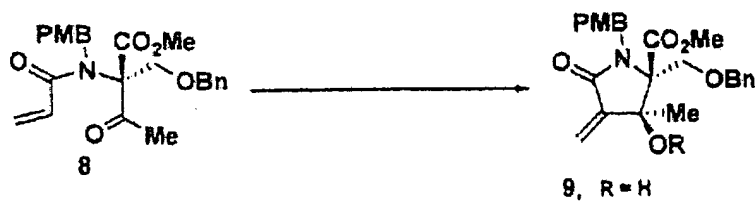
4. The intermediate step (d) of Claim 1, namely the acylation of 6 to afford the N-acrylyl-N-PMB derivative 7:



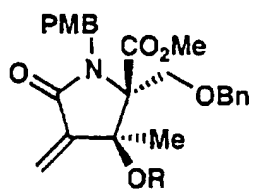
5. The intermediate step (e) of Claim 1, namely the oxidation of 7 to produce the keto amide ester 8:



6. The intermediate step (f) of Claim 1, namely the cyclization of 8 to afford the  $\gamma$ -lactam 9:



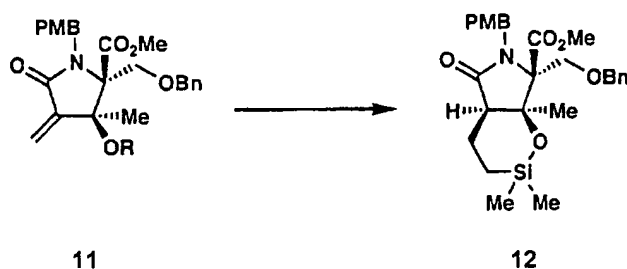
7. The intermediate step (g) of Claim 1, namely the silylation of 9 to produce the silyl ether 11:



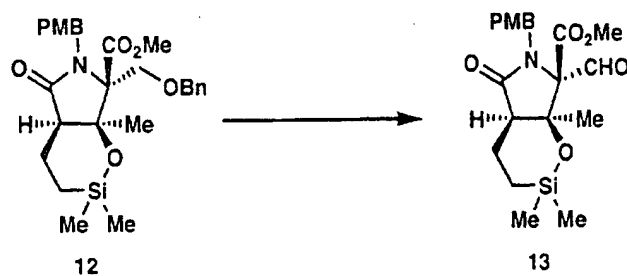
9, R = H

11, R = Si(Me)<sub>2</sub>CH<sub>2</sub>Br

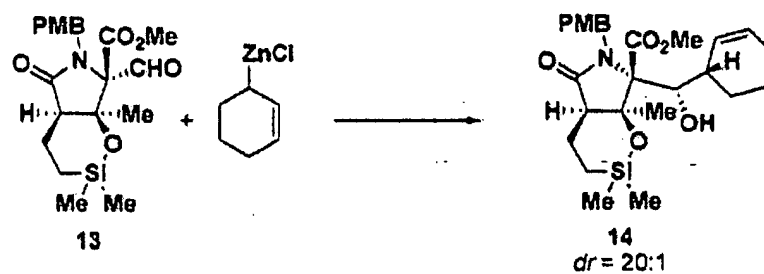
8. The intermediate step (h) of Claim 1, namely the cyclization of 11 to provide the *cis*-fused  $\gamma$ -lactam 12:



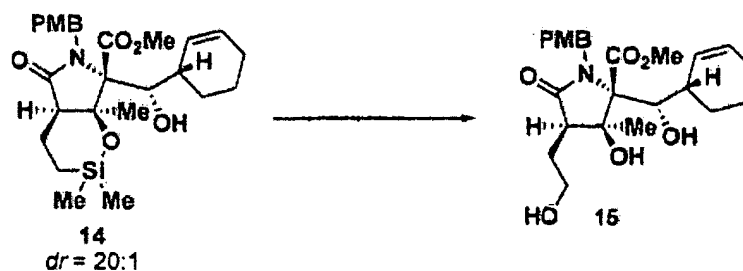
9. The intermediate step (i) of Claim 1, namely the oxidation of 12 to provide the aldehyde 13:



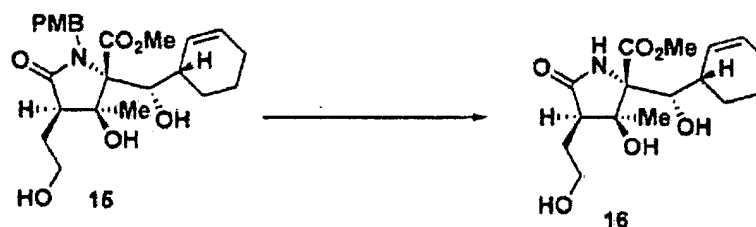
10. The intermediate step (j) of Claim 1, namely the reaction of 2-cyclo-hexenylzinc chloride with the aldehyde 13 to yield the formyl adduct 14:



11. The intermediate step (k) of Claim 1, namely the oxidation of 14 to provide the triol 15:

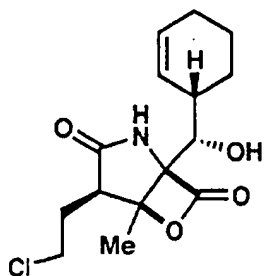
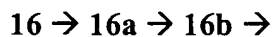


12. The intermediate step (l) of Claim 1, namely the cleaving the PMB group of 15 to yield the triol ester 16:





13. The intermediate step (m) of Claim 1, namely the hydrolysis of **16** to the corresponding  $\gamma$ -lactam-carboxylic acid **16a** (CO<sub>2</sub>Me in **16** is CO<sub>2</sub>H), followed by conversion of the acid **16a** to the beta-lactone **16b**, followed by conversion to salinosporamide A (**1**):



14. The synthetic intermediate compound of structure 5 in Claim 1.
15. The synthetic intermediate compound of structure 6 in Claim 1.
16. The synthetic intermediate compound of structure 7 in Claim 1.
17. The synthetic intermediate compound of structure 8 in Claim 1.
18. The synthetic intermediate compound of structure 9 in Claim 1.
19. The synthetic intermediate compound of structure 11 in Claim 1.
20. The synthetic intermediate compound of structure 12 in Claim 1.

21. The synthetic intermediate compound of structure 12a in Claim 1.
22. The synthetic intermediate compound of structure 13 in Claim 1.
23. The synthetic intermediate compound of structure 14 in Claim 1.
24. The synthetic intermediate compound of structure 15 in Claim 1.
25. The synthetic intermediate compound of structure 16 in Claim 1.
26. The synthetic intermediate compound of structure 16a in Claim 1.
27. The synthetic intermediate compound of structure 16b in Claim 1.